UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

Schwarz Pharma, Inc., Schwarz Pharma AG, and Warner-Lambert Company, LLC,

Plaintiffs,

v.

Paddock Laboratories, Inc.,

Defendant.

MEMORANDUM OPINION AND ORDER
Civ. No. 05-832 ADM/JJG

Brian M. Poissant, Esq., F. Dominic Cerrito, Esq., and Daniel L. Malone, Esq., Jones Day, New York, NY; and Laura J. Hein, Esq. and Peter R. Forrest, Esq., Gray, Plant, Mooty, Mooty & Bennett, P.A., Minneapolis, MN, argued on behalf of Plaintiffs.

Neil F. Greenblum, Esq., Michael J. Fink, Esq., Stephen M. Roylance, Esq., and P. Branko Pejic, Esq., Greenblum & Bernstein, P.L.C., Reston, VA; and Barbara P. Berens, Esq., Kelly & Berens, PA, Minneapolis, MN, argued on behalf of Defendant.

I. INTRODUCTION

The above-entitled matter is before the undersigned United States District Judge on Plaintiffs Schwarz Pharma, Inc., Schwarz Pharma AG, and Warner-Lambert Company, LLC's ("Plaintiffs") Motion to Alter or Amend Judgment Pursuant to Fed. R. Civ. P. 59(e) ("Rule 59(e) Motion") [Docket No. 229]. For the reasons stated herein, Plaintiffs' Motion is denied.

II. BACKGROUND

On October 20, 2006, summary judgment was granted for Defendant Paddock Laboratories, Inc. ("Paddock") and Judgment was entered. Order [Docket No. 222]; Judgment [Docket No. 224]. The Order discusses whether prosecution history estoppel bars Plaintiffs from relying on the doctrine of equivalents to establish infringement. The Court first concluded that argument-based prosecution history estoppel did not apply because the arguments made before

the Patent and Trademark Office did not evince a clear and unmistakable surrender of subject matter. Order at 8. The Court next examined amendment-based estoppel and found the patentee's amendment to the patent was a narrowing amendment made for a substantial reason related to patentability, resulting in the application of the presumption that the patentee surrendered all territory between the original claim limitation and the amended claim limitation. Order at 11. The Court further held that Plaintiffs were unable to rebut the presumption of total surrender because magnesium oxide was foreseeable as an equivalent to an alkali or alkaline earth metal carbonate[1] at the time of the narrowing amendment, and the rationale underlying the narrowing amendment was directly relevant to the equivalent in question. Order at 14-15. The Court concluded that amendment-based prosecution history estoppel applied, barring Plaintiffs from relying on the doctrine of equivalents to establish infringement, and granted summary judgment for Paddock. Plaintiffs then filed the instant Rule 59(e) Motion, arguing that the Court committed manifest errors of law and fact.

III. DISCUSSION

A. Rule 59(e)

In their Rule 59(e) Motion, Plaintiffs ask the Court to vacate its Order granting summary judgment for Paddock and to alter or amend the Judgment entered on October 20, 2006. Rule 59(e) simply states: "Any motion to alter or amend a judgment shall be filed no later than 10 days after entry of the judgment." Fed. R. Civ. P. 59(e). The practice of this district is to utilize Rule 59(e) motions to address mechanical changes to a judgment, such as correcting a dollar

[1] As Plaintiffs correctly point out, the Court's references to magnesium oxide being an equivalent to "magnesium carbonate" should instead have been magnesium oxide being an equivalent to "an alkali or alkaline earth metal carbonate."

amount that was incorrectly entered, and not to request the Court to reconsider the substance of a ruling. In this district, the vehicle to correct substantive errors is to ask leave to bring a motion to reconsider pursuant to Local Rule 7.1(g), which states:

> Motions to reconsider are prohibited except by express permission of the Court, which will be granted only upon a showing of compelling circumstances. Requests to make such a motion, and responses to such requests, shall be made by letter to the Court of no more than two pages in length, a copy of which must be sent to opposing counsel.

Plaintiffs have cited Eighth Circuit case law for the proposition that: "Although the words 'alter or amend' imply something less than 'set aside,' a court may use Rule 59(e) to set aside the entire judgment." Sanders v. Clemco Indus., 826 F.2d 161, 168 n.13 (8th Cir. 1988). Further, "Rule 59(e) motions serve a limited function of correcting 'manifest errors of law or fact or to present newly discovered evidence.' Such motions cannot be used to introduce new evidence, tender new legal theories, or raise arguments which could have been offered or raised prior to entry of judgment." Innovative Home Health Care, Inc. v. P.T.-O.T. Assocs. of the Black Hills, 141 F.3d 1284, 1286 (8th Cir. 1998) (internal citations omitted). Plaintiffs insist that their Motion is a Rule 59(e) motion because the Court has committed manifest errors of law and fact.

Plaintiffs' Motion does not conform to the local rules of practice and strikes the Court as an improper "second bite at the apple," as it raises the same arguments or arguments which could have been raised in the summary judgment context. See Dale & Selby Superette & Deli v. United States Dep't of Agric., 838 F. Supp. 1346, 1347-48 (D. Minn. 1993). However, because of the complexity of the case, and arguable support for Rule 59(e) being appropriate, the merits of the Motion will be addressed and the rationale for granting summary judgment to Paddock will be further explained.

B. Interchangeability

Because both parties take portions of the relevant cases out of context in order to justify their positions, an extended discussion of the relevant cases is warranted.

In Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 535 U.S. 722 (2002), the United States Supreme Court held that it is a patentee's burden to establish that a narrowing amendment to a patent does not surrender a particular equivalent. 535 U.S. at 740. The Supreme Court also stated that "[t]he patentee must show that at the time of the amendment one skilled in the art could not reasonably be expected to have drafted a claim that would have literally encompassed the alleged equivalent." Id. at 741. The Supreme Court then announced, without elaborating, three ways in which a patentee could rebut the presumption of total surrender: (1) by showing that the equivalent was unforeseeable at the time of the amendment, (2) by showing that the rationale underlying the amendment bears no more than a tangential relation to the equivalent in question, or (3) by showing that there is some other reason suggesting that the patentee could not reasonably be expected to have described the insubstantial substitute in question. Id. at 740-41. The Supreme Court remanded the case to the Federal Circuit for further proceedings, as the record then before the Supreme Court did not make it possible to determine whether the petitioner had "rebutted the presumptions that estoppel applies and that the equivalents at issue have been surrendered." Id. at 741.

On remand, the Federal Circuit examined "the proper roles of the judge and jury" with respect to rebuttal of the presumption of surrender. Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 344 F.3d 1359, 1367-68 (Fed. Cir. 2003). The Federal Circuit held that "rebuttal of the presumption of surrender is a question of law to be determined by the court, not a jury."

Id. at 1367. The court further stated: "We recognize that rebuttal of the presumption may be subject to underlying facts, which we discuss in more detail below. Nonetheless, the resolution of factual issues underlying a legal question may properly be decided by the court." Id. at 1368 n.3.

The Federal Circuit also examined the ways in which a party might establish the three types of rebuttal of the presumption of total surrender. The Federal Circuit then concluded: "Because we cannot anticipate all of the circumstances in which a patentee might rebut the presumption of surrender, we believe that discussion of the relevant factors encompassed by each of the rebuttal criteria is best left to development on a case-by-case basis. However, we provide the following general guidance . . . ." Id. at 1368. With respect to the foreseeability test, the Federal Circuit provided the following guidance:

> This criterion presents an objective inquiry, asking whether the alleged equivalent would have been unforeseeable to one of ordinary skill in the art at the time of the amendment. Usually, if the alleged equivalent represents later-developed technology (e.g., transistors in relation to vacuum tubes, or Velcro® in relation to fasteners) or technology that was not known in the relevant art, then it would not have been foreseeable. In contrast, old technology, while not always foreseeable, would more likely have been foreseeable. Indeed, if the alleged equivalent were known in the prior art in the field of the invention, it certainly should have been foreseeable at the time of the amendment. By its very nature, objective unforeseeability depends on underlying factual issues relating to, for example, the state of the art and the understanding of a hypothetical person of ordinary skill in the art at the time of the amendment. Therefore, in determining whether an alleged equivalent would have been unforeseeable, a district court may hear expert testimony and consider other extrinsic evidence relating to the relevant factual inquiries.

Id. at 1369. The Federal Circuit then attempted to apply its newly-elaborated-upon tests to the alleged equivalents at issue. The court ultimately determined that the record before it was not sufficiently developed to allow it to properly apply and evaluate the relevant tests, and remanded to the district court for further factual development. With respect to the first alleged equivalent,

the aluminum sleeve, the Federal Circuit said:

> First, we are unable to determine whether Festo can satisfy the first rebuttal criterion on the current record. Although it seems unlikely that an aluminum sleeve would have been unforeseeable, as it was made of a commonly available metal, Festo argues that one skilled in the art at the time of the "magnetizable" amendment would not have foreseen the interchangeability of an aluminum alloy sleeve and a magnetizable alloy sleeve in Stoll's small gap design involving rare earth magnets. Factual issues thus exist as to whether an ordinarily skilled artisan would have thought an aluminum sleeve to be an unforeseeable equivalent of a magnetizable sleeve in the context of the invention.

Id. at 1371. With respect to the second alleged equivalent, the sealing ring, the Federal Circuit said:

> First, we cannot determine from the current record whether the accused sealing ring element would have been objectively foreseeable at the time of the amendments. Festo argues that SMC's two-way sealing ring was an inferior and unforeseeable equivalent of the one-way sealing rings located at each end of the piston in the claimed invention. Factual issues thus exist as to whether a person of ordinary skill in the art would have considered the accused two-way sealing ring to be an unforeseeable equivalent of the recited pair of sealing rings.

Id. at 1372. Finally, the court stated, "On remand, both parties may introduce evidence relating to the unforeseeability of the equivalents in question, *as the trial court deems appropriate*." Id. at 1373 (emphasis added).

On remand to the district court, the court began by noting: "Ten years after trial, and following two sojourns to the Supreme Court, this seventeen-year-old suit is back on remand from the Federal Circuit." Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., No. Civ. A 88-1814, 2005 WL 1398528, at *1 (D. Mass. June 10, 2005). The court held a two-day bench trial in which two experts testified. Id. The court held that the plaintiff had not rebutted the presumption of surrender because both of the alleged equivalents would have been foreseeable to one of ordinary skill in the art at the time of the narrowing amendments, and entered judgment for the defendant. Id. The district court never once mentioned "interchangeability" at any point

in its opinion. The court found "the single sealing ring in the prior art German patent is strong evidence that use of a single sealing ring would have been foreseeable, in the context of the Festo device, to one of ordinary skill in the art at the time of the 1981 amendments." Id. at *6. The court also noted that because the German patent device used a non-magnetizable sleeve, "a non-magnetizable sleeve does not, in itself, constitute 'later-developed technology' and was 'known in the relevant art.'" Id. at *7 (internal citation omitted).

On January 29, 2004, the Federal Circuit decided companion cases Glaxo Wellcome, Inc. v. Impax Labs. Inc., 356 F.3d 1348 (Fed. Cir. 2004) and Smithkline Beecham Corp. v. Excel Pharms., Inc., 356 F.3d 1357 (Fed. Cir. 2004). Both cases concerned a patent directed to controlled sustained release tablets containing bupropion hydrochloride, with the key ingredient for achieving sustained release being hydroxypropyl methylcellulose ("HPMC"). Glaxo, 356 F.3d at 1349-50; Smithkline, 356 F.3d at 1359. In both cases, a drug manufacturer was attempting to market a generic version of the sustained release tablets containing bupropion hydrochloride that included a different key ingredient for achieving sustained release—hydroxypropyl cellulose ("HPC") in Glaxo and polyvinyl alcohol ("PVA") in Smithkline. Glaxo, 356 F.3d at 1351; Smithkline, 356 F.3d at 1360. In both cases, the court identified the "critical inquiry" as "whether Glaxo could have foreseen sustained release agents for bupropion other than HPMC at the time of filing or amendment." Glaxo, 356 F.3d at 1355; Smithkline, 356 F.3d at 1364.

In Glaxo, the court noted that neither party challenged the substantial equivalency of HPC and HPMC. 356 F.3d at 1351. However, the court did not simply accept this agreement in determining foreseeability. Instead, the court examined the record before it:

> On this point, the record shows that at the time the amendments were made, no known hydrogels other than HPMC had been tested with bupropion hydrochloride to achieve sustained release. Thus, with respect to bupropion alone, a portion of the record might suggest that HPC was not a known sustained release agent at the time of the amendment. The record, however, contains considerable evidence that suggests Glaxo could have described the sustained release compound HPC at the time the 798 patent claims were amended, if not earlier. In this regard, the record shows that both HPMC and HPC were known as sustained release hydrogel-forming polymers in the art of pharmaceutical formulation. For example, a 1994 pharmaceutical handbook teaches that both HPC and HPMC may serve as "an extended release tablet matrix." A 1962 patent claimed HPMC as a sustained release agent. Similarly a 1987 patent claimed HPC as a sustained release agent for a formulation using a solid tablet.

Id. at 1355 (internal citations omitted). The court then discussed other prior art references disclosed in Glaxo's Information Disclosure Statement to the Patent Office. Id. The court then concluded:

> This court, therefore, discerns from this record that ordinarily skilled artisans at the time would have considered HPC a suitable sustained release agent for bupropion. Indeed this court has scoured the record in vain for any evidence of a verifiable scientific reason that Glaxo would not have considered HPC a suitable sustained release agent for bupropion. As the district court also observed, the record shows only that "anyone skilled in the art [at the relevant time] would have known that HPC and HPMC were substantially equivalent." Accordingly, Glaxo has not rebutted the presumption that prosecution history estoppel bars a finding of infringement under the doctrine of equivalents.

Id. at 1355-56 (internal citation omitted). A fair reading of Glaxo reveals that the court did not simply rest on the plaintiff's failure to challenge the substantial equivalency of HPC and HPMC, and did not enter into any specific discussion about "interchangeability." Instead, the court looked at the entire record and found teachings in the Handbook of Pharmaceutical Excipients, prior patents that disclosed HPC and HPMC as sustained release agents, and references submitted by Glaxo to the Patent Office that described HPC, HPMC, and numerous other polymeric compounds as extended release drug formulations, were evidence that HPC was foreseeable as an equivalent. The Federal Circuit affirmed the district court's grant of summary

judgment for defendant.

In Smithkline, the court found the record before it insufficient to determine foreseeability:

> On this point, the record shows that at the time the amendments were made, no known hydrogels other than HPMC had been tested with bupropion hydrochloride to achieve sustained release. Thus, with respect to bupropion alone, a portion of the record might suggest that PVA was not a known sustained release agent at the time of the amendment. PVA later proved to work as a sustained release agent for bupropion, suggesting a[n] undeniable ground for unforeseeability, namely that PVA perhaps may qualify as a later-developed technology. Because the parties developed this record before the Supreme Court's Festo opinion with its doctrines for rebuttal of the presumption, this court cannot ascertain whether Glaxo should have foreseen PVA as a sustained release agent for bupropion and included it within its literal claims.
>
> This undeveloped record simply does not show whether ordinarily skilled artisans in this field at this time had verifiable scientific reasons to regard PVA as a foreseeable and claimable sustained release compound for bupropion or similar formulations. Glaxo relies on the declaration of its expert, Dr. Lowman, to support its contention that PVA and HPMC are functional equivalents in retarding the release of bupropion hydrochloride from an ingested tablet. However, the record does not disclose whether HPMC and PVA were recognized as interchangeable sustained release hydrogel-forming polymers used in the art of pharmaceutical formulation *at the time the claims were amended*. On this incomplete record, this court cannot discern whether the prior art disclosed PVA as an alternative to HPMC as a sustained release agent so that Glaxo could rationally foresee that a competitor might substitute PVA for HPMC in designing around the amended 798 patent claims or whether PVA was not a foreseeable sustained release agent for bupropion or similar formulations.
>
> In [Glaxo], a companion case issued today, this court discredited a foreseeability rebuttal for HPC in this exact field because the record abundantly disclosed that compound's use as a release agent at the relevant time. In contrast, this record for PVA does not permit a similar finding. Because foreseeability "depends on underlying factual issues," this court remands to facilitate development of the record on this key point. On remand, the trial court may inquire into the specific use of PVA in the prior art of sustained drug release compositions to ascertain whether artisans of ordinary skill in this art would have foreseen the potential substitution of PVA for HPMC at the time the 798 patent claims were amended.

Id. at 1364-65 (internal citation omitted) (emphasis added).

In the instant case, Plaintiffs first argue that the Court misinterpreted the Federal

Circuit's test for finding an alleged equivalent foreseeable at the time of the amendment to the patent. Plaintiffs essentially argue that the Court should have applied a mechanical, two-step test to determine foreseeability: First, the Court should determine whether the alleged equivalent is disclosed in the prior art. Second, if the first question is answered in the affirmative, the Court should determine whether at the time of the amendment, a person of ordinary skill in the art would have recognized the alleged equivalent to be interchangeable with the claim element in dispute given the context of the invention. Plaintiffs made essentially the same argument in their summary judgment opposition brief. Br. [Docket No. 183] at 18-32. The Court did not find the argument persuasive then, and does not find the argument persuasive now. The Federal Circuit has not announced an "interchangeability" test for the foreseeability analysis. Rather, words like "interchangeable" and "potential substitute" are alternative ways to describe equivalency. In fact, the Federal Circuit has described equivalent to mean "there is not a substantial difference between the claimed invention and the accused product." Pall Corp. v. Micron Separations, Inc., 66 F.3d 1211, 1218 (Fed. Cir. 1995).

The relevant factors to be considered in a foreseeability analysis are still being developed. The Federal Circuit has suggested in its relatively young precedent that a court, when conducting a foreseeability analysis, is to examine the entire record submitted by the parties, including the prior art, to determine whether the alleged equivalent was foreseeable to one of ordinary skill in the art at the time of the amendment. If the alleged equivalent is in the prior art, and is doing substantially the same thing in substantially the same way as the claim element at issue, then courts will find that it was foreseeable. In Glaxo, the court examined the record, including the teachings in the Handbook of Pharmaceutical Excipients, the prior patents

that disclosed the alleged equivalent and the claim element as sustained release agents, and the references submitted by the plaintiff to the Patent Office that described the alleged equivalent and the claim element as extended release drug formulations, plus the absence of a verifiable scientific reason that the plaintiff would not consider the alleged equivalent a suitable sustained release agent. Based on the examination, the court found the alleged equivalent was foreseeable. Glaxo, 356 F.3d at 1355-56.

In the instant case, the Court applied the same analysis as was done in Glaxo, and followed the Federal Circuit's precedents on foreseeability. The entire record submitted by both parties was examined, including the testimony of the experts in their declarations and depositions, the prior art patents, the entries in the Handbook of Pharmaceutical Excipients, and the experiments of the researchers. After analysis of the entire record, the alleged equivalent, magnesium oxide, was found to be foreseeable as an equivalent at the time of the amendment to an alkali or alkaline earth metal carbonate by one of ordinary skill in the art. Because this Court after reexamination still cannot discern a flaw in its interpretation and application of the Federal Circuit's precedent, any error will have to be determined by another court.

C. Plaintiffs' Evidence and the Court's Grant of Summary Judgment

Plaintiffs' also argue that the Court improperly failed to credit their evidence showing that one of ordinary skill in the art at the time of the amendment would not have recognized magnesium oxide to be an equivalent to an alkali or alkaline earth metal carbonate in the context of the invention, that there are genuine issues of material fact precluding summary judgment, and that the Court improperly made factual findings. Plaintiffs' must proffer competent evidence showing that there are genuine issues of material fact for trial, and Plaintiffs' have failed to meet

that burden.

In support of its Motion for Summary Judgment, Paddock supplied several prior art references to show that magnesium oxide was foreseeable as a stabilizer in the art of pharmaceutical formulation. Plaintiffs argued that Paddock's references were insufficient because they do not concern ACE inhibitors, they do not mention cyclization, and they do not all concern solid dosage forms. Plaintiffs countered with declarations and depositions of two experts to support their contentions while Paddock relied on the testimony of one expert.

Paddock relies principally on two Japanese patents. Japanese Patent S58-201710 ("JP '710") is directed toward "[a] stable intraoral amfenac paste preparation . . . ." Wiesner Decl. [Docket No. 185] Ex. 12. The "Description of the Invention" section of the JP '710 Patent states in relevant part:

> [W]hen an intraoral paste preparation containing amfenac salt is manufactured using the well-known blend shown in Table 1, the yellow color of the amfenac salt changes to orange-red when the preparation is stored at room temperature for one year. The generation of 7-benzoyl-2-oxyindole by the decomposition of amfenac salt has been confirmed by thin layer chromatographic analysis. When this type of amfenac paste preparation is manufactured by conventional well-known methods, production of preparations has been difficult due to this change in external appearance resulting from the generation of decomposition product and discoloration.
>
> The inventors of the present invention et al., as a result of repeated and painstaking investigations toward a solution to these problems, discovered that a stable preparation that does not discolor or decompose over time can be manufactured by adding one or more types of substance selected from magnesium oxide, basic magnesium carbonate and calcium carbonate in amounts that have no pharmacological effect on the amfenac salt. The present invention was perfected based on this discovery.

Id. Similarly, Japanese Patent S58-201726 ("JP '726") is directed toward "[a] method for preparing stable amfenac pharmaceutical by adding at least one selected from magnesium oxide, basic magnesium carbonate and calcium carbonate in an amount that does not have drug efficacy

to amfenac sodium and amfenac calcium." Pejic Decl. [Docket No. 178] Ex. 13. The "Description of the Invention" section states in relevant part:

> [W]hen these pharmaceuticals have been kept for one year under a room temperature airproof condition, the content of a capsule changed from a yellow color, which originates from amfenac sodium, to a light red color. In the case of tablets, the surface of a tablet changed from a yellow color to a red color. And in the case of powder, the color of the powder changed from yellow to light red. Further, it is confirmed by a thin-layer chromatography (TLC) analysis that 7-benzoyl-2-oxyindole, a main decomposed matter of amfenac sodium and amfenac calcium, has formed in all these pharmaceuticals. As described above, when amfenac pharmaceuticals are prepared by using the conventional public-known methods, because of the changes in appearance due to the formation of decomposed matter and the change in color, preparation of the pharmaceuticals is believed to be difficult.
>
> To address this problem, the inventors of the present invention, after conducting a series of researches on preparing pharmaceuticals that are stable with time, have discovered that, by adding at least one selected from magnesium oxide, basic magnesium carbonate and calcium carbonate in an amount that does not have drug efficacy to amfenac sodium and amfenac calcium, pharmaceuticals that do not change their color and are stable with time can be prepared. The present invention is completed based on this knowledge.

Id.

In his expert declaration, Paddock's expert Dr. Alekha K. Dash ("Dash") states:

> I note that Dr. Williams has not critically examined the structure of amfenac and its degradation product 7-benzoyl-2-oxyindole. If he had, he would appreciate and recognize that amfenac decomposes to 7-benzoyl-2-oxyindole via cyclization. Thus, amfenac is susceptible to cyclization and discoloration, or just cyclization.
>
> It is my opinion that the degradation from amfenac to 7-benzoyl-2-oxyindole can only occur via cyclization, which is clear by looking at the molecular structure of amfenac and the molecular structure of 7-benzoyl-2-oxyindole as shown below, wherein cyclization occurs by the reaction of the carboxylic group with the amino group to an amide.
>
> In view of the above, amfenac has the structural capability to cyclize via internal nucleophilic attack like certain ACE inhibitors. Therefore, it is my opinion that one of ordinary skill in the art would readily understand that amfenac degrades to 7-benzoyl-2-oxyindole by way of cyclization.
>
> Therefore, one of ordinary skill in the art knowledgeable of the teachings of the '710 and '726 patent documents would have known and understood that magnesium oxide (MgO)

> and magnesium carbonate were known stabilizers for pharmaceutical compositions to inhibit cyclization and discoloration. Therefore, at the time the Applicants amended the claims of the '450 patent application (i.e., November 11, 1987), one of ordinary skill in the art would have known and understood that magnesium oxide (MgO) could be used, i.e., it was foreseeable to use magnesium oxide (MgO) as a stabilizer to stabilize pharmaceutical compounds which have the structural capability to cyclize via internal nucleophilic attack, and/or discolor.

Dash Decl. [Docket No. 179] ¶¶ 67-70. In his expert declaration, Plaintiffs' expert Dr. Robert O. Williams III states:

> JP '710 describes 7-benzoyl-2-oxyindole as a decomposition product. It does not, however, provide any information as to what degradation pathway is responsible for the formation of this compound.
>
> In my opinion, JP '710 does not render the use of magnesium oxide to stabilize an ACE inhibitor against cyclization and discoloration, or just cyclization, foreseeable to a person of ordinary skill in the art as of November 11, 1987. As noted above, this reference does not concern ACE inhibitors. Thus, it does not teach how to stabilize an ACE inhibitor against cyclization and discoloration, or just cyclization. Moreover, as noted, JP '710 does not attribute the formation of 7-benzoyl-2-oxyindole to any particular degradation pathway. Additionally, the components of the amfenac paste are not the components one of ordinary skill in the art would use to form a solid dosage form, which the '450 patent describes as "highly preferred." In this regard, I further note that claim 12 of the '450 patent is specifically directed to a tablet. The fact that magnesium oxide in the presence of a set of components for making a paste may provide a stabilizing function for a nonsteroidal anti-inflammatory would not lead one of skill in the art to conclude that magnesium oxide in the presence of a different set of components (i.e., ones for making a solid dosage form) would stabilize an ACE inhibitor against cyclization and discoloration. This is particularly true where the claims of the '450 patent require the presence of a saccharide, which, in my opinion, the paste of JP '710 does not contain. The '450 patent also recognizes that the saccharide component could affect the functions of the other components of the formulation. (Col. 3, lines 50-54).
>
> I also note that JP '710 states explicitly that sodium carbonate and potassium carbonate do not stabilize the amfenac paste formulation. It further states that the "stabilization effect was found only with . . . divalent alkaline earth metals." Thus, JP '710 teaches that the "stabilization effect" is not found in amfenac formulations containing alkali metals. In contrast, the '450 patent teaches and claims the use of alkali metal carbonates (e.g., potassium carbonate and sodium carbonate) to stabilize ACE inhibitors against cyclization and discoloration. The fact that this class of materials does not perform a stabilization function in the amfenac formulations, but does in the claimed ACE inhibitor formulations, would lead one skilled in the art to conclude that these two formulations

> are simply too different to draw any conclusions regarding what role magnesium oxide might play in stabilizing an ACE inhibitor against cyclization and discoloration.
>
> ***
>
> In paragraph 68, Dr. Dash states that he believes that amfenac degrades by cyclization. However, Dr. Dash's opinion today regarding the degradation mechanism of amfenac is not relevant to the knowledge of one of ordinary skill in the art on November 11, 1987. In that regard, I note that neither of the JP References mentions cyclization as a degradation mechanism. I further note that neither reference concerns ACE inhibitors. Thus, in my opinion one of ordinary skill in the art at the time of the amendment would not have considered these references relevant when trying to solve the problem of stabilizing an ACE inhibitor against cyclization.

Williams Decl. [Docket No. 186] ¶¶ 27-31. Finally, Plaintiffs' expert Dr. George W. Gokel states in relevant part in his expert declaration:

> In my opinion, the JP references do not render the use of magnesium oxide foreseeable as a stabilizer of ACE inhibitors against cyclization and discoloration, or just cyclization, as of November 11, 1987. Cyclization is not discussed as a degradation mechanism although a degradation product identified is 7-benzoyl-2-oxyindole. I found no mention of ACE inhibitors, much less, the stability of ACE inhibitors. Thus, the JP references do not teach a person of ordinary skill how to stabilize ACE inhibitors against cyclization and discoloration.
>
> Dr. Dash states that it is his opinion that "the degradation from amfenac to 7-benzoyl-2-oxyindole can only occur via cyclization." (citation omitted). In my opinion, Dr. Dash's opinion regarding the possible degradation mechanisms of amfenac does not speak to what the JP references would have taught a person of ordinary skill in the art on November 11, 1987. One may surmise that cyclization in amfenac is possible but the aromatic amine nitrogen is far less nucleophilic than is the secondary aliphatic nitrogen of moexipril. Moreover, Dr. Dash appears to assert that cyclization leads automatically to discoloration. In my experience, reactions of classes of compounds must be determined on a case-by-case basis. Degradation is a chemical process and it must be understood to best prevent it. Even if it is not fully understood, stabilization must be determined experimentally for each class of compounds.
>
> In my opinion, one of ordinary skill in the art would not have considered the JP references relevant on November 11, 1987, when trying to solve the problem of stabilizing an ACE inhibitor against cyclization. As discussed above, the JP references concern amfenac, not ACE inhibitors. In my opinion, even if magnesium oxide could perform a stabilizing function in amfenac, the structure of amfenac is too different from the structures of ACE inhibitors, including quinapril and moexipril, to enable one skilled

> in the art to draw any meaningful conclusions from this regarding what role magnesium oxide might play in an ACE inhibitor formulation.
>
> I also note that the "stabilization effect" taught by JP '710 is not found in amfenac formulations containing alkali metals [i.e., potassium carbonate, kalium (potassium) carbonate, and sodium carbonate]. In contrast, the '450 patent teaches and claims the use of alkali metal carbonates to stabilize ACE inhibitors against cyclization and discoloration. I agree with Dr. Williams' opinion that the fact that this class of materials does not perform a stabilization function in the amfenac formulations, but does in the claimed ACE inhibitor formulations, would lead one skilled in the art to conclude that these two formulations are simply too different to draw any conclusions regarding what role magnesium oxide might play in stabilizing an ACE inhibitor against cyclization and discoloration. This is particularly true because the JP references do not contain a saccharide, and the '450 patent recognizes the potential for the saccharide component to interfere with the other components of the formulation. (citation omitted). In my opinion, the stabilization mechanisms in the two formulations are probably different. While amfenac's stability is based on the presence of divalent metals, the stability of the ACE inhibitors disclosed in the '450 patent cannot be based on this, since the claimed stabilizers do not all contain divalent metals. This indicates to me that magnesium oxide would not have been recognized to be interchangeable with the "alkali or alkaline earth metal carbonate" of the claimed invention by one of ordinary skill in the art on November 11, 1987.

Gokel Decl. [Docket No. 184] ¶¶ 24-27.

Plaintiffs stress that Paddock's references do not show magnesium oxide stabilizing against degradation by cyclization. Plaintiffs are correct that Paddock's references do not expressly use the word "cyclization." However, the Japanese patents both discuss magnesium oxide and magnesium carbonate as a stabilizer against discoloration and the decomposition product 7-benzoyl-2-oxyindole. Although Drs. Williams and Gokel state that the Japanese patents do not mention cyclization as a degradation mechanism, Dr. Dash explains that "degradation from amfenac to 7-benzoyl-2-oxyindole can only occur via cyclization, which is clear by looking at the molecular structure of amfenac and the molecular structure of 7-benzoyl-2-oxyindole." Dash Decl. ¶ 68. By rendering his "opinion," Dr. Dash is relying on verifiable scientific evidence, namely, the molecular structure of amfenac and its decomposition product.

Significantly, Dr. Williams, Plaintiffs' expert, agreed on cross examination that the degradation from amfenac to 7-benzoyl-2-oxyindole was the result of cyclization. Williams Dep. (Pejic Decl. Ex. 2) at 133 (A: "Magnesium oxide prevents formation of the decomposition product, the 7-benzoyl-2-oxyindole in the JP '710." Q: "Which is a result somewhere of cyclization?" A: "Cyclization from amfenac." Q: "Correct?" A: "Yes."). One of ordinary skill in the art will understand the structure of amfenac and the structure of its decomposition product, regardless of whether the word "cyclization" is specifically used.

Plaintiffs argue that Paddock's references are deficient because they do not specifically address ACE inhibitors. Plaintiffs' experts allege that the chemical structure of ACE inhibitors is too different from the chemical structure of amfenac to enable one skilled in the art to conclude that a stabilizer for amfenac might also function as a stabilizer for an ACE inhibitor. The Federal Circuit in Glaxo found a similar argument unavailing. The court determined that even though the record showed that at the time the amendments were made, no known hydrogels other than HPMC had been tested with bupropion hydrochloride to achieve sustained release, the record contained "considerable evidence that suggest[ed] that Glaxo could have described the sustained release compound HPC at the time the 798 patent claims were amended," including the teachings of the Handbook of Pharmaceutical Excipients, and other references that showed both HPC and HPMC as sustained release agents. Glaxo, 356 F.3d at 1355-56. Essentially, the court found that even though HPC had never been tested specifically with bupropion hydrochloride, it was foreseeable as a sustained release agent for bupropion hydrochloride.

In this case, prior references show magnesium oxide acting as a stabilizer against discoloration and cyclization with other active pharmaceutical ingredients. Under the Federal

Circuit's precedent, magnesium oxide, which is doing substantially the same thing in substantially the same way, is foreseeable as a potential substitute to an alkali or alkaline earth metal carbonate. As the district court in Festo found, the prior art patent, which shows magnesium oxide doing substantially the same thing in substantially the same way, is "strong evidence" that magnesium oxide would have been foreseeable, in the context of the '450 patent, to one of ordinary skill in the art at the time of the amendments. Festo, 2005 WL 13985298, at *6.[2]

Plaintiffs have a burden to come forward with competent evidence showing that there are genuine issues of material fact for trial. Plaintiffs also have the burden of rebutting the presumption of total surrender. Paddock supplied evidence to the Court establishing that at the time of the amendments, a person of ordinary skill in the art would have recognized magnesium oxide as a foreseeable equivalent to an alkali or alkaline earth metal carbonate given the context of the invention. While Plaintiffs' attorneys argued forcefully, skillfully, and tenaciously for their clients, Plaintiffs have failed to supply sufficient evidence to convince this District Judge that they have created a genuine issue of material fact for trial and to rebut the presumption of total surrender.

[2] Plaintiffs argue that the Handbook of Pharmaceutical Excipients describes magnesium oxide as a "diluent" and not a stabilizer, but that does not mean it can not also be a stabilizer. Wiesner Decl. Ex. 11.

IV. CONCLUSION

Based upon the foregoing, and all the files, records, and proceedings herein, **IT IS HEREBY ORDERED** that Plaintiffs' Rule 59(e) Motion to Alter or Amend Judgment Pursuant to Fed. R. Civ. P. 59(e) ("Rule 59(e) Motion") [Docket No. 229] is **DENIED**.

BY THE COURT:

s/Ann D. Montgomery
ANN D. MONTGOMERY
U.S. DISTRICT JUDGE

Dated: November 20, 2006.